Outcome and recurrence one year after paediatric arterial ischaemic stroke in a population-based cohort

Running Head : Outcome after paediatric arterial ischaemic stroke

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Abstract

Objective:

Arterial ischaemic stroke (AIS) is an important cause of acquired brain injury in children. Few prospective population-based studies of childhood AIS have been completed. We aimed to investigate the outcome of childhood AIS 12 months after the event in a population-based cohort.

Methods:

Children aged 29 days to less than 16 years with radiologically confirmed AIS occurring over a 1-year period residing in southern England (population 5.99 million children) were eligible for inclusion. Outcome was assessed during a home-visit using the Paediatric Stroke Outcome Measure (PSOM). Parental impressions of recovery were assessed using the Paediatric Stroke Recurrence and Recovery Questionnaire (RRQ). PSOM score was estimated via telephone interview or clinician interview whenever home-visit was not possible.

Results:

96 children with AIS were identified. 2 children were lost to follow-up. 9/94 (10%) of children died before the 12-month follow-up. One child had an AIS recurrence. PSOM scores were available for 78 of 85 living children at follow-up. 39/78 (50%) had a good outcome (total PSOM score <1) and 39/78 (50%) had a poor outcome. Seizures at onset of AIS were associated with a poor outcome (Odds Ratio 3.5 95% CI 1.16-10.6). 28/73 (38%) children were judged by their carers to have fully recovered. 10/84 (12%) of children had recurrent seizures and 17/84 (20%) reported recurrent headaches.

Interpretation:

AIS carries a significant risk of mortality and long-term neurological deficit. However, the rates of mortality, recurrence and neurological impairment were markedly lower in this study than previously published figures in the UK.

Introduction

The incidence of arterial ischemic stroke (AIS) in children in the United Kingdom is 1.6 per 100,000 per year.[1] The range of risk factors associated with AIS in children is very wide and they are different from those typically associated with AIS in adults.[1, 2] Another critical difference from adults is that the ischaemic insult occurs in a developing brain. There is a paucity of outcome data and, in particular, there are very few data describing outcome following childhood AIS on a population-basis. Outcome assessment in previous studies has almost exclusively been performed in series of children based in single hospitals, typically specialist centres, and this is recognised as a potential source of selection bias towards more severe cases.[3] In studies of stroke in adults hospital-based cohorts have been shown to include more severe strokes and have higher mortality rates than population-based cohorts.[4] In addition to the lack of population-based data many paediatric studies have assessed outcome using ad hoc, author-generated outcome measures making comparisons between studies difficult.[5] There are now two outcome measures that have been prospectively validated for use in paediatric AIS.[6, 7]

Outcome data are required for prognostication and estimating the risk of recurrence. There is growing interest in developing clinical trials for childhood AIS[8-10] and robust outcome data are essential to inform the efficient design of such trials. Such outcome data will be key drivers of the need to find effective acute treatments, secondary prevention measures, and rehabilitative therapies. There are considerable economic costs associated with the acute care of children with AIS and lifelong costs for a child are likely to be substantially higher than for an adult given the longer life expectancy.[11] Characterisation of the outcome of childhood stroke will focus rehabilitation and direct allocation of resources such as psychology, physiotherapy and occupational therapy.

The aim of this study was to assess the outcome one year after AIS in a population-based cohort of children.

Methods

Study Design and Participants

Children aged 29 days to less than 16 years with radiologically confirmed AIS occurring between July 1, 2008 and June 30, 2009 and residing in southern England (population 5·99 million children) were eligible for inclusion. Cases were identified using multiple sources to maximise ascertainment as previously reported[1] and were confirmed by personal examination and note review. All cases were identified within the UK's comprehensive National Health Service (NHS) by active surveillance involving a wide range of health professionals, a paediatric neurology rare disease surveillance system, a paediatric intensive care surveillance system, and direct notification from parents or carers.

AIS was defined as acute neurological symptoms secondary to acute focal cerebral infarction in an arterial distribution on brain imaging. Recurrence was recorded if a new acute neurological deficit with further cerebral infarction occurred after the index stroke.

Risk factors, the presenting features, and radiological features of AIS were categorised using the International Paediatric Stroke Study (IPSS) scheme.[2, 12] Stroke subtype was categorised according to the Childhood AIS Standardised Classification and Diagnostic Evaluation (CASCADE) criteria.[13] As this was an observational study the researchers did not direct the investigation of risk factors or stroke subtype. Therefore, an additional CASCADE category of "undetermined etiology without complete workup" was used to classify cases where the etiology was unclear but there had not been complete investigation (including echocardiogram, MRI, and vascular imaging of the head and neck). Infarct topography was recorded according to involvement of brain structures (cerebral cortex, subcortical white matter, basal ganglia, posterior limb of the internal capsule, thalamus, cerebellum, and brainstem). Vascular territory was recorded as anterior or posterior and small artery or large artery.

Details of acute treatments (defined as the medical management any time during the initial hospitalisation for AIS) and treatment on discharge were also recorded in line with IPSS practice.[14] Antithrombotic therapies were subdivided into antiplatelet therapies (aspirin, clopidogrel, dipyridamole, or others) and anticoagulant therapies (unfractionated or low molecular weight heparin, warfarin, or others).

Outcome was assessed by a researcher during a home visit or by telephone one year after the index AIS. For those families unwilling to be contacted by a researcher outcome was assessed by the local clinician.

The study was granted multi-centre ethical approval from Southampton & South West Hampshire Research Ethics Committee (B) and site specific approval at all National Health Service trusts within the study area.

Procedures

Details of presenting features, risk factors, radiological features, and acute treatments were obtained from the medical case notes including those cases that died prior to follow-up.

A paediatrician trained in the use of the Paediatric Stroke Outcome Measure (PSOM) assessed outcome during a home visit, 12 to 13 months following the AIS. The PSOM is a validated tool for assessing clinical neurological outcome following paediatric AIS.[6] Neurological deficits are categorised into 5 spheres; right sensorimotor, left sensorimotor, language production (expressive language); language comprehension (receptive language), and cognitive-behavioural deficits. An ordinal score of 0 to 2 is assigned to these spheres where 0 = no deficit, 0·5 = mild deficit with normal function, 1 = moderate impairment with decreased function, and 2 = severe deficit with missing function. The PSOM total score (tPSOM) is the sum of the 5 subscale scores and ranges from

0 (no deficit) to 10 (maximum deficit). A good outcome was considered a tPSOM < 1 and a poor outcome a tPSOM $\geq$ 1 or death due to AIS or contributed to by AIS.[15]

Parental impressions of recovery were assessed using the Paediatric Stroke Recurrence and Recovery Questionnaire (RRQ), which is validated for use in paediatric AIS.[7] The RRQ was also used to assess AIS recurrence and the presence of headaches and recurrent seizures at follow-up. Recurrent seizures were defined as more than one unprovoked seizure in the 6 months prior to the follow-up assessment. Recurrence was also assessed by review of medical records and radiological investigations. The RRQ was also used for participants requesting a telephone interview and for participants no longer resident in the UK or Channel Islands.

Clinician interview was used to assess outcome in the small number of children where home visit or telephone consultation was not possible. In these cases outcome was based upon the clinicians' review of the medical records relating to clinical assessment closest to 12 months post-AIS. PSOM scores estimated by review of medical records have previously been found to closely match "live, in-clinic" assessments.[6]

The study was observational and the clinical care of the children was at the discretion of the treating physician.

Statistical Analysis

In univariable analyses, Fisher's exact test was used for comparison of categorical variables and Wilcoxon-Mann-Whitney rank sum test for continuous variables.

Logistic regression models were fitted to assess relationships between outcome and presenting features, risk factors, and radiological features. Logistic regression analyses were conducted with a penalised maximum likelihood estimation approach using the Firth method[16, 17] to reduce bias for

small sample sizes.[18, 19] All logistic regression analyses were adjusted for age, sex, and race as these were considered, *a priori,* to be factors that may be associated with outcome. Age at stroke onset in years was treated as a continuous variable in logistic regression analyses. Following Kim[20] we treated the deaths as a competing risk for AIS in the estimation of the recurrence rate. We used the R package `cmprsk`[21] to compute the cumulative incidence function. Though not strictly correct, we also report the Kaplan-Meier estimate of the recurrence rate at 12 months treating deaths as independent censoring events, for comparison to the rest of the literature.

For all statistical testing, α was set at 0·05. Statistical analyses were performed using Stata IC 11·2 (Statacorp, College Station, Texas, USA) and R version 3.1.2 (R Foundation for Statistical Computing, Vienna).

Role of the Funding Source

The funding source had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The study identified 96 children with AIS. Their features are summarised in Table 1 and stroke subtype according to CASCADE criteria in Table 2. Nine children died before follow-up. 69 children and their families agreed to a home visit but 2 were lost to follow-up by the researchers leaving 67 children assessed at home. Outcome was assessed in six cases by telephone interview (parental preference in 5 cases and due to emigration from the UK in 1 case). Outcome was assessed by clinician interview in 12 cases but was not fully known in one case.

Death and Discharge

9/94 (10%) children died during the follow-up period. Four children died during the acute admission related to the AIS and 1 child was discharged home for palliative care and died 2 days later. The remaining 4 children were discharged and died at times remote (greater than 30 days) from the index AIS (Figure 1).

All children who died had at least one risk factor for AIS identified and 7/9 had multiple risk factors. Four children had haematological malignancies and one had an intracranial tumour. Five children had acute infections (meningitis, septicaemia, or pneumonia). Two children had congenital heart disease and one child was on ECMO. The AIS was considered to be the cause of death or contributing to death in four cases. The primary cause of death was a relapsed haematological malignancy in three cases, an intrancranial tumour in one case, and pneumonia in one child with severe congenital cyanotic heart disease.

The time to discharge from hospital or to death (if in hospital) was known in 90/94 children. The median time to discharge or death in hospital (calculated from cases in whom the time was known) was 13·5 days (IQR 6 - 27 days).

Recurrence

One child had a radiologically confirmed recurrent AIS in the follow-up period, giving a recurrence rate of 1/94 (1%). The single case of recurrent AIS occurred 81 days after the first AIS. The child was on warfarin therapy for a vertebral artery dissection. It was not known if recurrence had occurred in the two cases lost to follow-up.

The Kaplan-Meier estimate of recurrence at 12 months considering deaths as independent censoring is 0.011; the competing risk model yields an estimated recurrence rate of 0.0106.

Treatment

Data on acute treatments were available on all children. All eight children with sickle cell disease (SCD) had acute exchange transfusions. 51/96 (53%) children had antiplatelet therapy alone, eight (8%) had anticoagulation therapy alone, 11 (11%) had both antiplatelet and anticoagulation therapy (includes children receiving both drug types at any time during acute hospitalisation, not necessarily concurrently) and 26 (27%) had neither. Two children received intra-arterial stents. There were no surgical revascularisation procedures during the 12 month follow-up period. One child was administered intravenous tissue plasminogen activator (tPA), commencing 4·5 hours after symptom onset. No complications of tPA were reported but the outcome was poor (tPSOM score 3·5). One child with a posterior circulation stroke and confirmed basilar artery occlusion secondary to vertebral artery dissection had mechanical thrombectomy 6·5 hours after symptom onset. The child also received intra-arterial tPA delivered directly into the thrombus. No complications were reported and outcome was good (tPSOM 0·5). One child with radiographic evidence of small-vessel vasculitis was treated with intravenous methylprednisolone and then oral prednisolone. One child received dexamethasone acutely due to concerns about raised intracranial pressure. Two other children received steroids and other immunomodulating drugs in the acute period following their AIS as treatment for other underlying conditions (inflammatory bowel disease and complications of bone marrow transplantation).

On discharge 57/96 (59%) had antiplatelet therapy alone, 11 (11%) had anticoagulation therapy alone, 2 (2%) had both and 26 (27%) had neither.

Parental Impressions of Recovery

RRQ data was available on 73 children of 85 living children: 67 assessed during the home visit and 6 by telephone. Using the RRQ 28/73 (38%) children were judged by their carers to have fully recovered. Of 45/73 that did not make a full recovery 26/45 (58%) required extra help with day-to-day activities compared with children of the same age. In the physician-assessed group 4/11 (36%) were judged to have fully recovered.

Seizures

Data on seizures were available on 84/85 children alive and remaining in follow-up at one year. 10/84 (12%) children had recurrent seizures at follow-up. 9/84 (11%) of children were taking regular anti-epileptic drugs (AEDs) of which 8 had recurrent seizures. One child taking regular AEDs had had seizures on day three post-AIS but none since. Two children with recurrent seizures were not taking regular AEDs at follow-up. In a multivariate regression analysis, age at AIS, sex, race, and the presence of cortical infarction were not associated with seizures at follow-up but seizures at onset of AIS were associated with later seizures, (odds ratio 10·4, 95% CI 1·8 - 39·4; p=0·007; n=84).

Headache

Data on headaches were available on 84/85 children alive and remaining in follow-up at one year. 17/84 (20%) children were experiencing headaches at follow-up. 11/17 (65%) were male. Both headache at onset of AIS (OR 3·6, 95% CI 1·1 - 12·5; p=0·040; n=84) and age at AIS onset (OR 1·12, 95% CI 1·00 - 1·26; p=0·048; n=84) were independently associated with headache at follow-up although gender was not associated.

Paediatric Stroke Outcome Measure

PSOM scores were available for 78 children of 85 living children: 67 assessed at home visit and 11 assessed by interview of treating physician. Demographic features and outcomes were similar between the researcher-assessed cases and the treating physician assessed cases (Table 3).

The median tPSOM score for the 78 cases was 0·75 (IQR 0 - 2). The maximum score was 10. The distribution of scores is shown in Figure 2. 34/78 (44%) had a score of zero and 39/78 (50%) had a tPSOM <1. A tPSOM ≥1 was seen in 39/78 (50%) cases. Neurological deficits were most frequently identified in the sensorimotor domains (Figure 3) with 31/78 (40%) children having a score ≥ 1 in either the left or right sensorimotor domains.

Combining children in whom a PSOM score was known and those children where AIS was considered to be the cause of death or contributing to death, 39/82 (48%) had a good outcome (tPSOM <1) and 43/82 (52%) had a poor outcome (tPSOM ≥ 1 or death due to AIS or contributed to by AIS). Dichotomised outcome did not vary according to the demographic features of age at AIS, sex, or race (Table 3). Increasing time to discharge or death in hospital (in days) was associated with a poor outcome, OR 1·035 (95% CI 1·004 - 1·066); *p*=0·025; *n*=78 (adjusted for age, sex, and gender, and only including cases in whom the time was known in this analysis).

Seizures at onset of AIS were associated with a poor outcome, OR 3·50 (95% CI 1·16 to 10·6), p = 0·026 (Table 5). Recurrent seizures at follow-up may be associated with a poor outcome, OR 5·84 (95% CI 0·95 - 35·70), *p*=0·056, *n*=78 (adjusted for age, sex, and race). Analyses of the relationships

between risk factors for AIS and outcome showed that arteriopathy was associated with lower odds of a poor outcome (Table 6). No statistically significant associations between radiological features and outcome were identified (Table 7). However, all eight children with a pattern of infarction involving the cerebral cortex, subcortical white matter, basal ganglia and posterior limb of the internal capsule had a poor outcome. Finally, outcome was not associated with use of antithrombotic therapy (antiplatelet and/or anticoagulation); OR 1·56 (95% CI 0·49 - 5·00), p=0·46, n=82 (adjusted for age, sex, and race).

Discussion

This prospective population-based study describes the outcome following paediatric AIS. It avoids the selection biases inherent in specialist centre-based studies, and it has used validated outcome measures. A potential weakness is that the 12 month follow-up is relatively short and we may have missed either some deficits yet to become apparent or some late recurrences. Whilst deficits in some domains may be apparent at 12 months following AIS other deficits may not become apparent until the child fails to meet certain developmental milestones. In particular, cognitive deficits may be difficult to detect in very young children. Furthermore, although this is the largest population based study of childhood AIS in the literature, the numbers for statistical analysis are still relatively small and some predictors of outcome may have been missed.

The most widely cited UK study of outcome following childhood AIS reported a poor outcome in 60% of non-neonatal children even though it did not include deaths.[22] Our study, demonstrates a poor outcome in 50% of children assessed at one year, rising to 52% if deaths attributable to AIS are included. The better outcomes documented in this study may have been due to lack of selection bias or because treatment has improved in the last decade. The outcomes that we demonstrated were

closer to those in an outcome study from Toronto although that study too was not population based and, therefore, susceptible to some selection bias.[23]

The 10% case fatality rate found in this study is lower than the approximately 15% rate reported by previous studies.[22, 24-26] Fewer than half of the deaths were attributable to the AIS. The majority of mortality in childhood AIS is due to pre-existing critical illness. Childhood stroke in the context of pre-existing critical illness has been reported to be a marker of increased mortality risk.[27] The lower overall case fatality rate found in this cohort compared to historical cohorts may represent improved care for a range of critical illnesses. The 4% in-hospital case fatality rate is similar to the 3% mortality rate before hospital discharge reported in a recent IPSS cohort.[14]

The one-year recurrence risk of AIS in this study was 1%. This is lower than the 15% - 20% rates reported by most large studies[24, 28, 29] although one study reported a rate of 6·6%.[30] Previous studies used longer follow-up periods (up to a median of 5 years)[29] although the majority of recurrence occurs within the first 12 months. The low recurrence rate seen in this study may be due to the lack of selection bias or it may reflect differences in treatment. The distribution of stroke subtypes in his study may be indicative of the lack of selection bias and be a factor in explaining the low recurrence risk. Various studies have found the highest recurrence rates in children with moyamoya.[28-30] In this study only 2% of cases had excessive collateral vessels versus moyamoya being found in 13%-14% of cases in studies reporting higher rates of recurrence.[28-30] The aim of antithrombotic treatment is to reduce the risk of recurrence although none of the three largest studies reporting recurrence rates following childhood AIS have found that such therapy was associated with the risk of recurrence.[28-30] However, no study of childhood AIS has treated children with antithrombotic therapy in a controlled manner and it is likely that antithrombotic treatments were given to children judged to be at higher risk of recurrence. The proportion of children given antithrombotic therapy (excluding children with SCD) in the three largest studies reporting recurrence rates was 45% - 55% versus 73% for this cohort. The children described in the previous studies had the index AIS between 1978 - 2004 and

the higher rates of antithrombotic use in the current cohort may be due to improving recognition of those most likely to benefit from antithrombotic therapy over time.

Children are at higher risk of post-stroke epilepsy than adults.[31, 32] Younger age is associated with acute seizures at presentation of AIS[1] and this may be because the immature brain has enhanced excitability favouring seizure propagation in the context of acute injury.[33] Acute seizures and possibly recurrent seizures are associated with a poor outcome. It is not clear if seizures are a marker for more severe brain injury or seizures themselves, as well anti-epileptic drug treatments, impair recovery.[32] Nevertheless, the high risk of seizures in childhood AIS must be recognised as this is a potentially modifiable aspect of post-stoke treatment.

Greater brain plasticity in the young has been suggested as a reason why they should recover better from brain injury than older children.[34] However, there is growing evidence that there are critical periods for neurodevelopment in early life that render very young children particularly vulnerable to brain insult.[35] In this study the worst outcome was found in the children with AIS in infancy; 69% of children aged under 1 year had a poor outcome versus 49% for older children.

In this study arteriopathy was associated with a good outcome. This contrasts with IPSS data that found arteriopathy was associated (OR 1·83, 95% CI 1·16 - 2·89) with a poor early (at discharge) outcome.[14] However, arteriopathy is an umbrella term covering a diverse group of conditions including arterial dissection, moyamoya, focal cerebral arteriopathy, and post-varicella arteriopathy.[1, 2] Different arteriopathies are associated with different outcomes and recurrence rates. Progressive types such as moyamoya tend to have worse outcomes.[36] Different distributions of types of arteriopathy across studies may account for varied reported outcomes. Studies from specialist centres will have a greater proportion of patients with progressive arteriopathies. For example, the widely cited UK study that reported a 60% poor outcome rate identified moyamoya as a risk factor for AIS in 19% of the cases. In this current study only 4% of cases had bilateral cerebral arteriopathy and only 2% had excessive collaterals.

Infarction involving multiple brain structures was common in this study so examining the effects of single sites on outcome was difficult. In a previous study of 43 children with AIS 9/11 (82%) with involvement of the cerebral cortex, basal ganglia, and posterior limb of the internal capsule had hemiparesis at follow-up.[37] A further study found worse neurological deficit in children with infarction involving the cortex, subcortical white matter, and thalamus.[38] In our study infarction involving a combination of cerebral cortex, subcortical white matter, basal ganglia and posterior limb of the internal capsule had a universally poor outcome. However, a poor outcome was also seen with a wide range of other infarction patterns.

This study, because it is population based, is more generalizable than most previous studies of AIS. It has shown that whilst many will have a residual deficit 12 months after their stroke, nearly 50% will make an almost complete recovery. It demonstrates that both mortality and recurrence rate at 12 months is lower than has previously been published. It casts doubt on the idea that stroke at an earlier age (< 1 year) is associated with a better outcome and it re-emphasises that both seizures at the onset of the stroke and a particular pattern of radiological injury involving the cortex, subcortical white matter, basal ganglia and posterior limb of the internal capsule are bad prognostic signs. The results of this study, because it has used the previously validated PSOM which is now gaining widespread international acceptance, should be a resource for comparison with future studies performed in different countries and at different times.

Acknowledgments

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Authorship

The study was conceived by FJO, VG, and FJK and designed by FJO, VG, FJK, and AAM. AAM, SA, and HBE collected the data. AAM, FJO, and MC-B completed the statistical analyses. All authors reviewed and revised the manuscript and all authors approved the final draft. The study was supervised by FJO.

Potential Conflicts of Interest

The authors declare there are no conflicts of interest.

Figures

Figure 1. Kaplan-Meier plot showing survival against time from AIS onset.

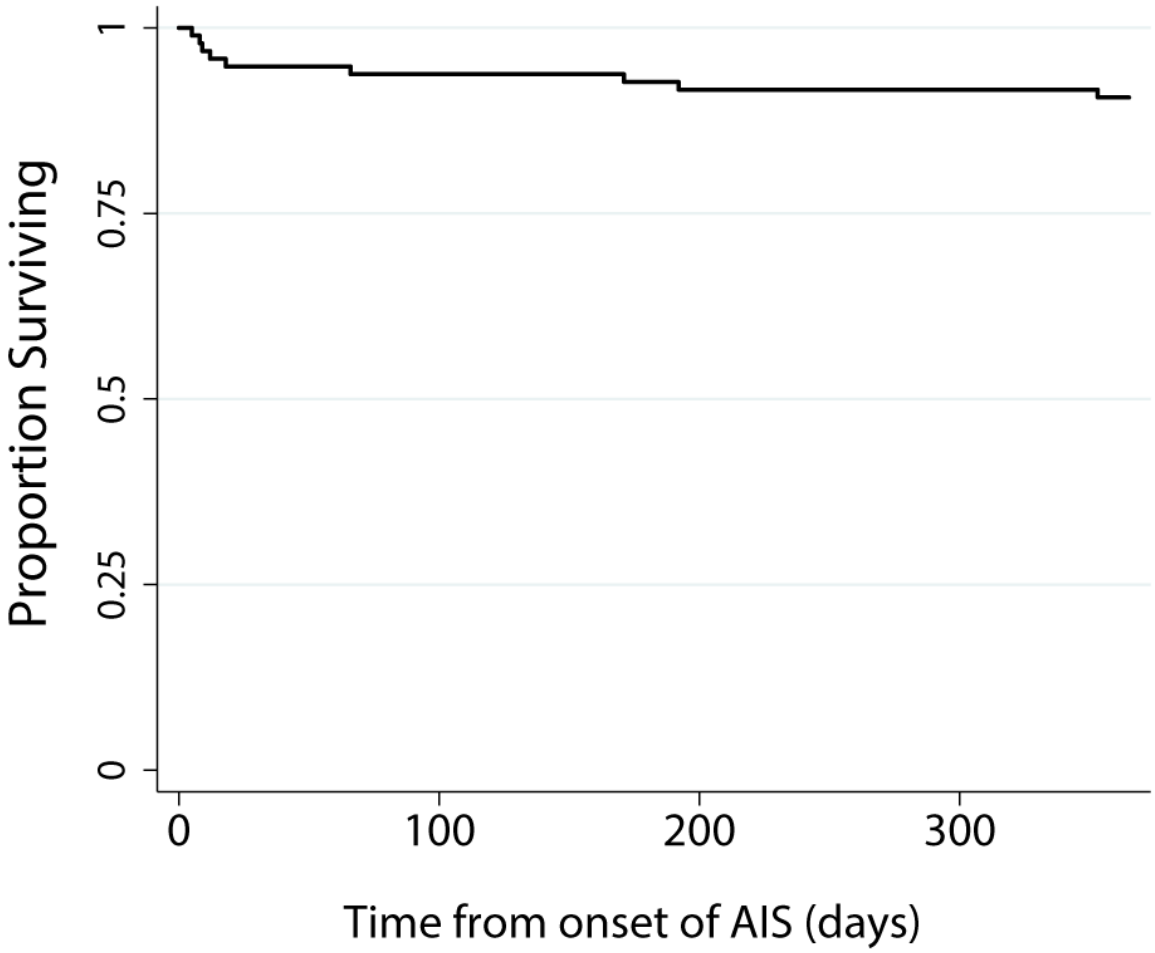


Figure 2. Distribution of total PSOM scores.

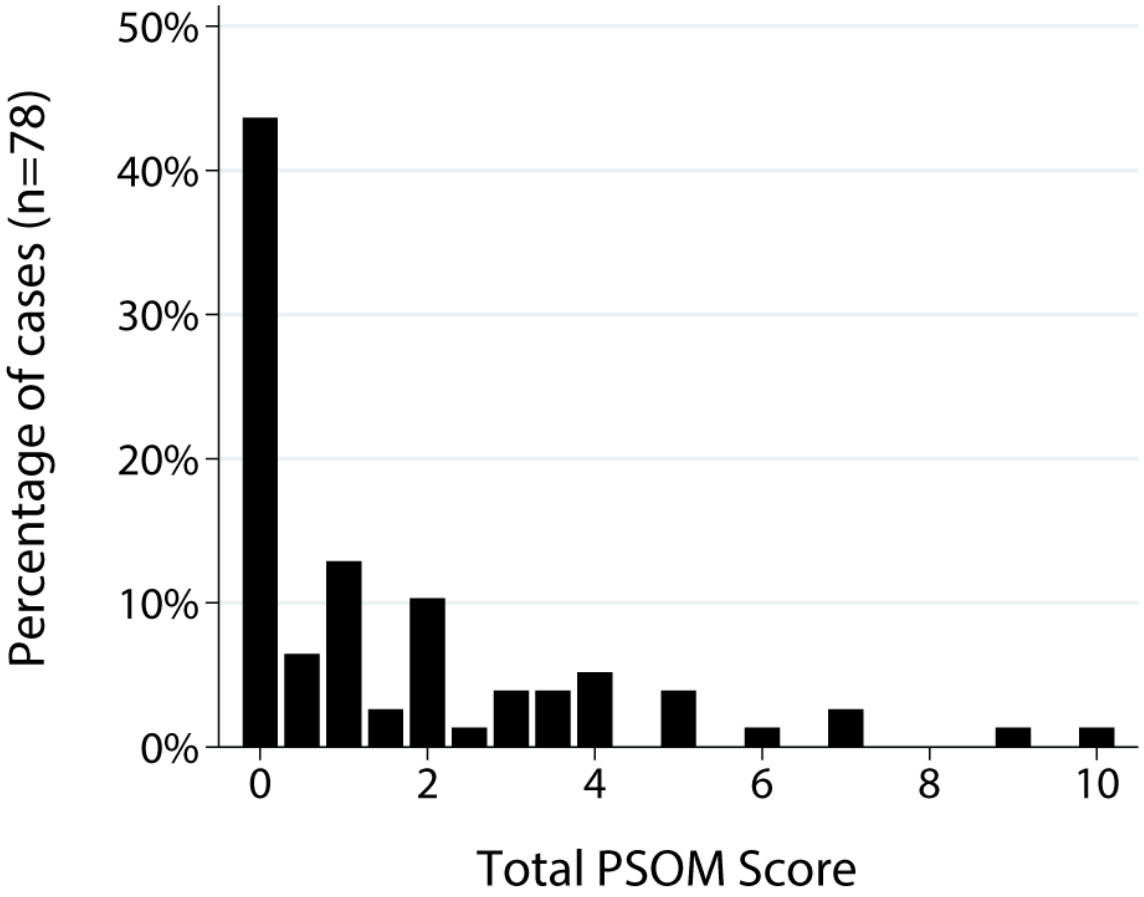
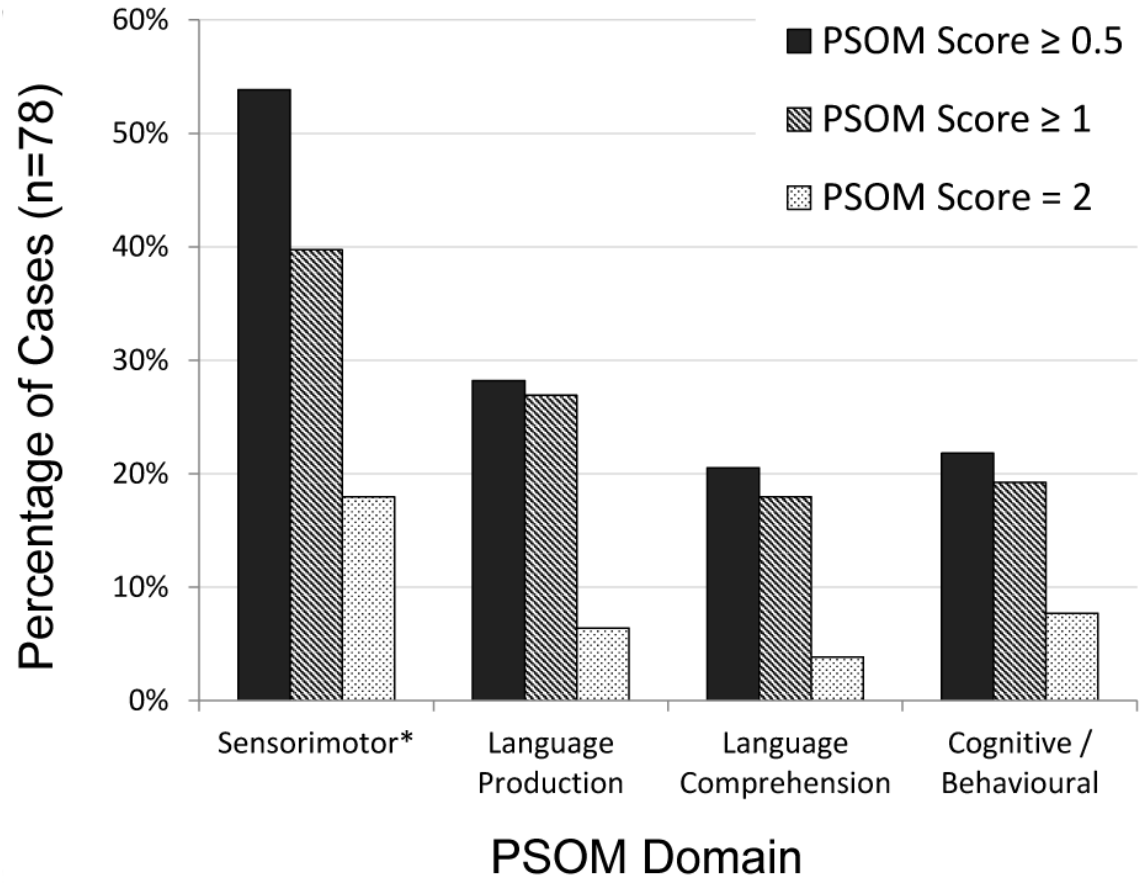


Figure 3. Distribution of PSOM scores showing neurological deficits according to domain.



Tables

Table 1. Features of whole cohort of 96 children.

Feature	Number of cases (%)
Age	
<1 year	16 (17%)
1 – 5 years	47 (49%)
6 – 10 years	10 (10%)
11 – 15 years	23 (24%)
Sex	
Male	49 (51%)
Female	47 (49%)
Race	
White	66 (69%)
Asian	14 (15%)
Black	9 (9%)
Other	7 (7%)
Presenting Features	
Focal features	82 (85%)
Diffuse features	59 (61%)
Seizures	28 (29%)
Risk Factors	
Acute systemic	30 (31%)
Arteriopathy	28 (29%)
Chronic systemic	24 (25%)
Cardiac	22 (23%)
Acute head and neck	18 (19%)
Prothrombotic state	5 (5%)
Recent infection	4 (4%)
Chronic head and neck	4 (4%)
Adult atherosclerosis risks	2 (2%)
No risk factor	16 (17%)
Acute Antithrombotic Treatment	
Antiplatelet alone	51 (53%)
Anticoagulation alone	8 (8%)
Antiplatelet and anticoagulation	11 (11%)
No antiplatelet or anticoagulation	26 (27%)

Table 2. Stroke subtype (CASCADE criteria).

CASCADE primary classification	Number of cases (%)
Small-vessel arteriopathy	17 (18%)
Radiographic	1 (1%)
Probable	16 (17%)
Unilateral focal-cerebral arteriopathy	18 (19%)
Anterior circulation without collaterals	17 (18%)
Posterior circulation	1 (1%)
Bilateral cerebral arteriopathy	4 (4%)
With collaterals	2 (2%)
Without collaterals	2 (2%)
Aortic/Cervical arteriopathy	6 (6%)
Dissection	6 (6%)
Cardio-embolic	20 (21%)
Definite	18 (19%)
Probable	2 (2%)
Other	29 (30%)
Undetermined etiology with complete workup	14 (15%)
Other	8 (8%)
Undetermined etiology without complete workup	7 (7%)
Multi-factorial	2 (2%)

Table 3. Demographic features and total PSOM scores according to type of follow-up.

	Researcher Assessed Outcome ***n*=73**	**Treating Physician Assessed Outcome** ***n*=12**	**p**
Median age at AIS in completed years (IQR)	4 (1 – 8)	4 (1 – 12.5)	0.63
Male	38 (52%)	5 (42%)	0.55
Race			
White	53 (73%)	7 (58%)	0.32
Asian	7 (10%)	3 (25%)	0.15
Black	7 (10%)	2 (17%)	0.61
Other	6 (8%)	0 (0%)	0.59
Median total PSOM score (IQR)	0.5 (0 - 2.5) [*n*=67]	1 (0 - 2) [*n*=11]	0.92

Table 4. Relationship of demographic features to outcome (*n*=82).

	Poor Outcome Number Cases (Percentage)		
Demographic Feature	**No**	**Yes**	**p**
Age			0.59
<1 year	4 (31%)	9 (69%)	
1 – 5 years	21 (49%)	22 (51%)	
6 – 10 years	4 (50%)	4 (50%)	
11 – 15 years	10 (56%)	8 (44%)	
Sex			1.00
Male	20 (47%)	23 (53%)	
Female	19 (49%)	20 (51%)	
Race			0.90
White	29 (48%)	32 (52%)	
Asian	3 (38%)	5 (63%)	
Black	4 (50%)	4 (50%)	
Other	3 (60%)	2 (40%)	

Table 5. Logistic regression analysis assessing relationship between poor outcome and presenting features adjusted for age, sex, and race (*n*=82).

Presenting Feature (n = number exhibiting that feature*)	**Odds Ratio (95% CI)**	**p**
Focal features (*n*=71)	0.39 (0.10 – 1.51)	0.17
Diffuse features (*n*=48)	1.62 (0.65 – 4.01)	0.30
Seizures (*n*=22)	3.50 (1.16 – 10.6)	0.026
Reduced conscious level (*n*=34)	2.27 (0.91 – 5.64)	0.078

* Overall number of cases in each analysis is 82 but number exhibiting each feature shown for information.

Table 6. Logistic regression analysis assessing relationship between poor outcome and risk factors for AIS adjusted for age, sex, and race (*n*=82).

Risk Factor (n = number exhibiting that feature*)	**Odds Ratio (95% CI)**	**p**
Acute systemic (*n*=24)	1.48 (0.54 – 4.09)	0.45
Arteriopathy (*n*=27)	0.31 (0.11 – 0.86)	0.024
Chronic systemic (*n*=19)	0.90 (0.24 – 3.37)	0.87
Cardiac (*n*=17)	2.55 (0.80 – 8.14)	0.12
Acute head and neck (*n*=14)	0.76 (0.23 – 2.40)	0.64
Idiopathic (no risk factors identified) (*n*=15)	1.03 (0.34 – 3.15)	0.95
Single Risk Factor (*n*=30)	2.07 (0.79 – 5.43)	0.14
Multiple Risk Factors (*n*=37)	0.48 (0.19 – 1.23)	0.13

* Overall number of cases in each analysis is 82 but number exhibiting each feature shown for information.

Table 7. Logistic regression analysis assessing relationship between poor outcome and radiological features adjusted for age, sex, and race (*n*=82).

Radiological Pattern or Features (*n* = number exhibiting that feature*)	**Odds Ratio (95% CI)**	***p***
CC, WM (*n*=12)	0.65 (0.17 – 2.75)	0.51
BG (*n*=12)	0.85 (0.25 – 2.85)	0.79
CC, WM, BG, PLIC (*n*=8)	17.3 (0.95 – 315)	0.054
CC, WM, BG (*n*=7)	4.46 (0.66 – 29.9)	0.12
WM (*n*=7)	0.95 (0.20 – 4.41)	0.95
WM, BG (*n*=7)	0.58 (0.12 – 2.69)	0.48
CC (*n*=6)	1.61 (0.31 – 8.33)	0.57
Multiple infarcts (*n*=27)	0.59 (0.23 – 1.48)	0.26
Bilateral infarcts (*n*=15)	1.03 (0.33 – 3.18)	0.96
Multiple (but not bilateral infarcts) (*n*=12)	0.38 (0.11 – 1.32)	0.13
Small vessel territory (*n*=53)	0.77 (0.31 – 1.94)	0.58
Large vessel territory (*n*=34)	1.40 (0.56 – 3.47)	0.47
Anterior circulation (*n*=73)	1.87 (0.45 - 7.69)	0.39
Posterior circulation (*n*=23)	0.89 (0.34 - 2.31)	0.81

CC = Cerebral cortex
WM = Subcortical white matter
BG = Basal ganglia
PLIC = Posterior limb of the internal capsule

* Overall number of cases in each analysis is 82 but number exhibiting each feature shown for information.

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